

10/509,732

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("6380258").PN.	US-PGPUB; USPAT	OR	OFF	2007/07/01 20:42
L2	1	("7115632").PN.	US-PGPUB; USPAT	OR	OFF	2007/07/01 22:44
L3	389	(544/383,514/252.12,514/255.01). CCLS.	US-PGPUB; USPAT	OR	OFF	2007/07/01 22:52
L4	38	I3 and carbamic adj acid	US-PGPUB; USPAT	OR	ON	2007/07/01 22:53
L5	0	I4 and hdac	US-PGPUB; USPAT	OR	ON	2007/07/01 22:55
L6	37	I4 and (phenyl or aryl)	US-PGPUB; USPAT	OR	ON	2007/07/01 22:56
L7	32	I6 and carbonyl	US-PGPUB; USPAT	OR	ON	2007/07/01 22:58
L8	27	I7 and sulfonyl	US-PGPUB; USPAT	OR	ON	2007/07/01 22:58

10/509,732 search after election

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NEWS 11 APR 30 INPADOC replaced by INPADOCDB on STN  
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NEWS 13 MAY 08 CA/Caplus Indian patent publication number format defined  
NEWS 14 MAY 14 RDISCLOSURE on STN Easy enhanced with new search and display fields  
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NEWS 16 MAY 21 TOXCENTER enhanced with BIOSIS reload  
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NEWS 18 MAY 22 CA/Caplus enhanced with IPC reclassification in Japanese patents  
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NEWS 20 JUN 29 STN Viewer now available  
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L3 82 SEA SSS FUL L1

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	ENTRY	SESSION
FULL ESTIMATED COST	172.10	172.31

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L4 25 L3

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L4 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2007:441608 CAPLUS

TITLE: A quantitative structure-activity relationship study on matrix metalloproteinase inhibitors: piperidine sulfonamide aryl hydroxamic acid analogs

AUTHOR(S): Kumaran, S.; Gupta, S. P.

CORPORATE SOURCE: Department of Pharmacy, Birla Institute of Technology and Science, Pilani, 333031, India

SOURCE: Journal of Enzyme Inhibition and Medicinal Chemistry (2007), 22(1), 23-27

CODEN: JETMAZ; ISSN: 1475-6366

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A quant. structure-activity relationship (QSAR) study has been made on a series of piperidine sulfonamide aryl hydroxamic acid analogs acting as matrix metalloproteinase (MMP) inhibitors. The inhibitory potencies of the compds. against two MMPs, MMP-2 and MMP-13, are found to be significantly correlated with the hydrophobic properties of the mols., suggesting that in both enzymes the hydrophobic interaction is playing a dominant role.

IT 309385-85-5  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

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FILE 'HOME' ENTERED AT 20:54:27 ON 01 JUL 2007

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 29 JUN 2007 HIGHEST RN 940349-93-9  
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L1 STRUCTURE UPLOADED

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SAMPLE SEARCH INITIATED 20:54:56 FILE 'REGISTRY'  
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100.0% PROCESSED	394 ITERATIONS	5 ANSWERS
SEARCH TIME: 00.00.01		

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 6690 TO 9070  
PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

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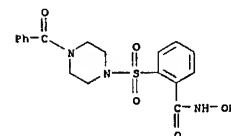
100.0% PROCESSED	7671 ITERATIONS	82 ANSWERS
SEARCH TIME: 00.00.01		

<12/04/2007>

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(Biological study); PRP (Properties)  
(QSAR study on inhibitors of matrix metalloproteinases 2 and 13)  
RN 309385-85-5 CAPLUS  
CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2007:216815 CAPLUS

DOCUMENT NUMBER: 146:434176

TITLE: Novel Selective Inhibitors of the Zinc Plasmodial Aminopeptidase PfA-M1 as Potential Antimalarial Agents

AUTHOR(S): Filipo, Marion; Beghyn, Terence; Leroux, Virginie; Florent, Isabelle; Deprez, Benoit P.; Deprez-Poulain, Rebecca F.

CORPORATE SOURCE: Biostructures and Drug Discovery, Inserm U761, Lille, F-59006, Fr.

SOURCE: Journal of Medicinal Chemistry (2007), 50(6), 1322-1334

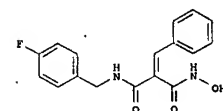
CODEN: JMCMAZ; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

Q1



AB Proteases that are expressed during the erythrocytic stage of Plasmodium falciparum are newly explored drug targets for the treatment of malaria. The authors report here the discovery of potent inhibitors of PfA-M1, a metallo-aminopeptidase of the parasite. These compds. are based on a malonic hydroxamic template and present a very good selectivity toward neutral aminopeptidase (APN-CD13), a related protease in mammals. Structure-activity relationships in these series are described. Further

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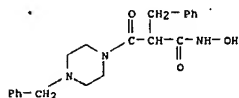
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optimization of the best inhibitor yielded a nanomolar, selective inhibitor of PfA-M1 (1). This inhibitor displays good physicochem. and pharmacokinetic properties and a promising antimalarial activity.

IT 934618-87-8P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (selective inhibitors of zinc plasmaloid aminopeptidase PfA-M1 as potential antimalarial agents)

RN 934618-87-8 CAPLUS  
 CN 1-Piperazinepropanamide, N-hydroxy-β-oxo-α,4-bis(phenylmethyl)- (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2006:1245530 CAPLUS  
 DOCUMENT NUMBER: 146:155298  
 TITLE: A library of novel hydroxamic acids targeting the metallo-protease family: Design, parallel synthesis and screening  
 AUTHOR(S): Flipo, Marion; Beghyn, Terence; Charton, Julie; Leroux, Virginie A.; Deprez, Benoit P.; Deprez-Poulain, Rebecca F.  
 CORPORATE SOURCE: Inserm, U761, Faculty of Pharmacy, Inst. Pasteur Lille, Lille, F-59006, Fr.  
 SOURCE: Bioorganic & Medicinal Chemistry (2007), 15(1), 63-76  
 CODEN: BMECEP; ISSN: 0968-0896  
 PUBLISHER: Elsevier Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The authors report here the design and parallel synthesis of 217 compds. based on a malonic-hydroxamic acid template. These compds. are obtained via a two-step solution-phase procedure. The set of diverse building-blocks used makes this strategy suitable for the search of inhibitors of various metallo-proteases and for the investigation of the biol. role of new metallo-proteases. As a proof of concept, the authors screened this library on neutral aminopeptidase (APN; E.C. 3.4.11.2), the prototypal enzyme of the M1 family. Several submicromolar inhibitors were identified.

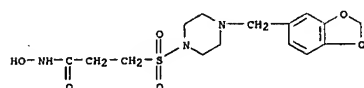
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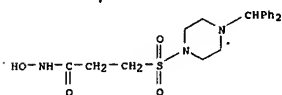
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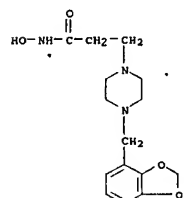
hydroxy- (CA INDEX NAME)



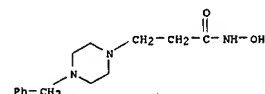
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 CN Propanamide, 3-[[4-(diphenylmethyl)-1-piperazinyl]sulfonyl]-N-hydroxy- (CA INDEX NAME)



RN 919997-21-0 CAPLUS  
 CN 1-Piperazinepropanamide, 4-(1,3-benzodioxol-5-ylmethyl)-N-hydroxy- (CA INDEX NAME)



RN 919997-22-1 CAPLUS  
 CN 1-Piperazinepropanamide, N-hydroxy-4-(phenylmethyl)- (CA INDEX NAME)



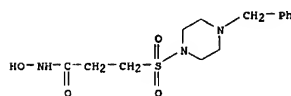
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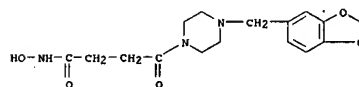
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(design, parallel synthesis and screening of hydroxamic acids targeting the metallo-protease)

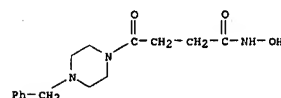
RN 260438-45-7 CAPLUS  
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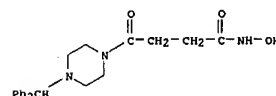
RN 919996-11-5 CAPLUS  
 CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-N-hydroxy-γ-oxo- (CA INDEX NAME)



RN 919996-12-6 CAPLUS  
 CN 1-Piperazinebutanamide, N-hydroxy-γ-oxo-4-(phenylmethyl)- (CA INDEX NAME)



RN 919996-19-3 CAPLUS  
 CN 1-Piperazinebutanamide, 4-(diphenylmethyl)-N-hydroxy-γ-oxo- (CA INDEX NAME)



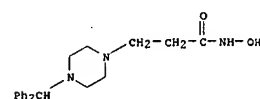
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&lt;12/04/2007&gt;

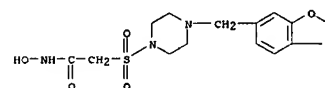
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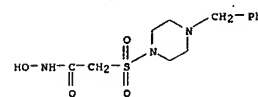
RN 919997-29-8 CAPLUS  
 CN 1-Piperazinepropanamide, 4-(diphenylmethyl)-N-hydroxy- (CA INDEX NAME)



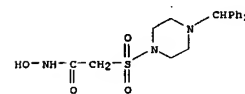
RN 919997-57-2 CAPLUS  
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RN 919997-58-3 CAPLUS  
 CN Acetamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (CA INDEX NAME)



RN 919997-65-2 CAPLUS  
 CN Acetamide, 2-[[4-(diphenylmethyl)-1-piperazinyl]sulfonyl]-N-hydroxy- (CA INDEX NAME)

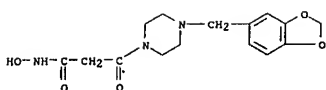


RN 919997-97-0 CAPLUS  
 CN 1-Piperazinepropanamide, 4-(1,3-benzodioxol-5-ylmethyl)-N-hydroxy-β-oxo- (CA INDEX NAME)

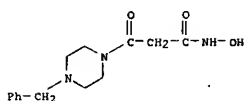
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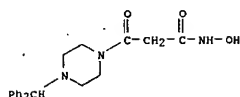
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RN 919997-99-2 CAPLUS  
CN 1-Piperazinepropanamide, N-hydroxy-β-oxo-4-(phenylmethyl)- (CA INDEX NAME)



RN 919998-10-0 CAPLUS  
CN 1-Piperazinepropanamide, 4-(diphenylmethyl)-N-hydroxy-β-oxo- (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2006:1024194 CAPLUS  
DOCUMENT NUMBER: 145:397368  
TITLE: Preparation of sulfonyl aryl or heteroaryl hydroxamic acid compounds as matrix metalloprotease inhibitors  
INVENTOR(S): Bedell, Louis J.; McDonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Shashidhar, Rao N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.  
PATENT ASSIGNEE(S): U.S. 163pp., Cont.-in-part of U.S. Ser. No. 310,813.  
SOURCE: CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 11  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7115632	B1	20061003	US 2000-569034	20000511

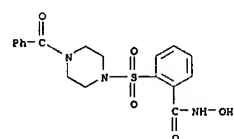
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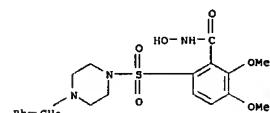
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MMP-13. Also disclosed is a treatment process that comprises administering a contemplated sulfonyl aromatic or heteroarom. ring hydroxamic acid compound in a matrix metalloprotease (MMP) enzyme-inhibiting effective amount to a host having a condition associated with pathol. MMP activity.  
IT 308385-85-5P 308385-86-6P 308385-87-7P  
RI: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

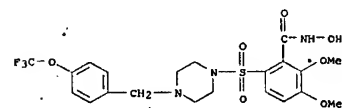
(preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as matrix metalloprotease inhibitors)  
RN 308385-85-5 CAPLUS  
CN Benzamide, 2-[[4-(benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 308385-86-6 CAPLUS  
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS  
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl)sulfonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS

&lt;12/04/2007&gt;

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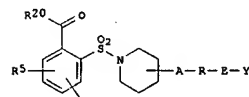
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US 2001020021 A1 20010906 US 1999-230209 19990624  
US 6380258 B2 20020430  
US 2001085680 A2 20011115 WO 2001-0514706 20010507  
WO 2001085680 A3 20020207  
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US 1999-310813 B2 19990512  
US 1999-230209 A2 19990624  
US 1997-35182P P 19970304  
WO 1998-054300 M 19980304  
US 2000-569034 A 20000511  
US 2000-728408 A2 20001201

OTHER SOURCE(S): MARPAT 145:397368  
OI



AB The title compds. [I; A = O, S, CO<sub>2</sub>, etc.; R = alkyl, alkoxyalkyl, aryl, etc.; E = CO, SO<sub>2</sub>, (un)substituted CONH, etc.; Y = H, alkyl, alkoxy, etc.; R<sub>5</sub>, R<sub>6</sub> = H, alkyl, cycloalkyl, etc.; R<sub>20</sub> = OR<sub>21</sub>, NR<sub>10</sub>R<sub>22</sub>, etc. (R<sub>13</sub> = H, alkyl, benzyl; R<sub>21</sub> = alkyl, aryl, arylalkyl; R<sub>22</sub> = selectively removable protecting group)] or pharmaceutically acceptable salts thereof that inter alia inhibit matrix metalloprotease activity, are prepared. Thus, thioetherification of 4-phenoxypheylthio)benzaldehyde with 2-fluorobenzaldehyde in the presence of K<sub>2</sub>CO<sub>3</sub> in isopropanol under reflux for 20 h gave 2-(4-phenoxypheylthio)benzaldehyde which was condensed with tetra-ethyl dimethylaminomethylenediphosphonate in the presence of NaH in THF at room temperature for 4 h gave to 2-[[2-(4-phenoxypheylthio)phenyl]acetic acid (III). II was oxidized by H<sub>2</sub>O<sub>2</sub> in acetic acid to 2-[[2-(4-phenoxypheylthio)phenyl]acetic acid which was condensed with 0-tetrahydropyran-2-ylhydroxylamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in MeCN followed by treatment with p-toluenesulfonic acid in methanol at room temperature for 2 h to give N-hydroxy-2-[[2-(4-phenoxypheylthio)phenyl]acetamide (III). III and N-hydroxy-2,3-dimethoxy-6-[[4-(4-(trifluoromethyl)phenoxy]-1-piperidinyl)sulfonyl]benzamide showed IC<sub>50</sub> of >10,000 nM against MMP-1, 0.3 and 2.4 nM, resp., against MMP-2, and 2 and 2.7 nM, resp., against

&lt;12/04/2007&gt;

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RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

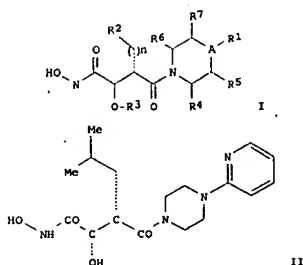
L4 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2006:101557 CAPLUS  
DOCUMENT NUMBER: 144:171021  
TITLE: Preparation of piperazine and related N-hydroxy succinic acid diamide derivatives as metalloproteinase inhibitors with therapeutic uses  
INVENTOR(S): Swinnen, Dominique; Bombrun, Agnes; Gonzalez, Jerome; Croisigant, Stefano; Gerber, Patrick; Jorand-Lebrun, Catherine  
PATENT ASSIGNEE(S): Applied Research Systems Ars Holding N.V., Neth. Antilles  
SOURCE: PCT Int. Appl., 203 pp.  
CODEN: PIAKX2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010751	A1	20060202	WO 2005-EP53616	20050725
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BO, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, GU, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GG, GW, ML, MR, NE, SN, TD, TG, BM, GH, GM, KE, LS, MW, ME, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005266313 A1 20060202 AU 2005-266313 20050725				
CA 2570903 A1 20060202 CA 2005-2570903 20050725				
EP 1771421 A1 20070411 EP 2005-772035 20050725				
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 1989106 A 20070627 CN 2005-80025086 20050725				
IN 2006DN07460 A 20070622 IN 2006-DN7460 20061211				
NO 2007000994 A 20070426 NO 2007-994 20070221				
PRIORITY APPLN. INFO.:				
EP 2004-103574 A 20040726				
US 2004-59111P P 20040726				
EP 2005-100641 A 20050311				
US 2005-648924P P 20050201				
WO 2005-EP53616 W 20050725				

OTHER SOURCE(S): MARPAT 144:171021  
OI

&lt;12/04/2007&gt;

Erich Leese



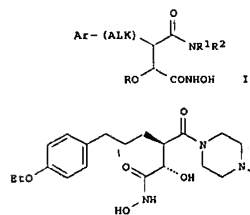
AB The present invention is related to piperazine and related N-hydroxy succinic acid diamide derivs. (shown as I, variables defined below; e.g. (2S,3S)-N-hydroxy-2-hydroxy-5-methyl-3-[(4-(2-pyridinyl)-1-piperazinyl)carbonyl]hexanamide (shown as II)) and use thereof, in particular for the treatment and/or prophylaxis of autoimmune disorders, inflammatory diseases, cardiovascular diseases, neurodegenerative diseases, cancer, respiratory diseases and fibrosis, including multiple sclerosis, arthritis, emphysema, chronic obstructive pulmonary disease, liver and pulmonary fibrosis. A = -C(=O)- and N, B is H or B forms a bond with either R5 or R7; R' = H, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, C3-C8-cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C3-C8-cycloalkyl C1-C6 alkyl, heterocycloalkyl C1-C6 alkyl, heteroaryl C1-C6 alkyl, amino and alkoxy; R2 = H, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, C3-C8-cycloalkyl, heterocycloalkyl, alkoxy, aryl and heteroaryl; R3 = H, C1-C6 alkyl, C2-C6 alkenyl and C2-C6 alkynyl; R4, R5, R6 and R7 = H, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl; or R4 and R7 form together a -CH2- linkage; n is an integer = 1, 2, 3, 4, 5 and 6; Carbons (2) and (3) are two chiral centers, wherein chiral center (2) has a configuration = S and R and wherein chiral center (3) has a S configuration as well as pharmaceutically acceptable salts thereof. Methods of preparation are claimed and preps. and/or characterization data for approx. 90 examples of I are included. For example, II was prepared from a 55/45 mixture of (2S)- and (2R)-pentafluorophenyl 2-[(4S)-2,2-dimethyl-5-oxo-1,3-dioxolan-4-yl]-4-methylpentanoate (preparation by partial diastereoisomerization of latter isomer) by 1st creating an amide linkage using 1-(2-pyridyl)piperazine (40 %) and then a 2nd amide linkage using hydroxylamine (31 %). IC50 values for inhibition of MMP-1, MMP-9 and MMP-12 by 16 examples of I are tabulated. Also, percentage of inhibition of IL-2-induced peritoneal recruitment of lymphocytes (model for cellular migration that occurs during inflammation) by 8 examples of I are tabulated.

IT 874646-99-8P, (2S,3R)-6-(4-Ethoxyphenyl)-N-hydroxy-2-hydroxy-3-[(4-(2-morpholin-4-yl)ethyl)piperazin-1-yl]carbonyl]hexanamide  
874647-38-8P, (2S,3R)-6-(4-Ethoxyphenyl)-N-hydroxy-2-hydroxy-3-[(4-(2-(2-thienylethyl)piperazin-1-yl)carbonyl]hexanamide  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

&lt;12/04/2007&gt;

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WO 2005019194	A1	20050303	WO 2004-GB3558	20040818
W: AE, AO, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HK, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BM, BH, BM, GM, GR, KE, LB, MG, MN, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, BG, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, MD, MR, NE, SN, TD, TO				
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CA 2536576	A1	20050303	CA 2004-2536576	20040818
EP 1660471	A1	20060531	EP 2004-768117	20040818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007503422	T	20070222	JP 2006-524410	20040818
CN 1930139	A	20070314	CN 2004-80023748	20040818
US 2006001302	A	20060519	NO 2006-1302	20060322
IN 2006CH00997	A	20070615	IN 2006-CH997	20060323
US 2006281920	A1	20061214	US 2006-568433	20060808
PRIORITY APPLN. INFO.:			GB 2003-19917	A 20030823
			GB 2003-28632	A 20031210
			WO 2004-GB3558	N 20040818
OTHER SOURCE(S):			CASREACT 142:280227; MARPAT 142:280227	
GI				



AB Title compds. I [wherein Ar = (un)substituted (hetero)aryl or (hetero)cycloalkyl; R = H or (cyclo)alkyl; Alk = alkylene or alkenylene; R1 and R2 link together to form (un)substituted heterocycloalkyl rings which is optionally fused to (un)substituted (hetero)cycloalkyl rings; and enantiomers, diastereoisomers, salts, hydrates or solvates thereof] were prepared as inhibitors of matrix metalloproteinases. For example, II was synthesized starting from (2S)-hydroxybutyric acid diisopropyl ester in several steps, which showed inhibitory activity against MMP-9, MMP-2, MMP-1 and MMP-12 with IC50 values of <100 nM, <100 nM, >10000 nM, <100 nM, resp. II also showed 57% inhibition of IL2-induced peritoneal recruitment

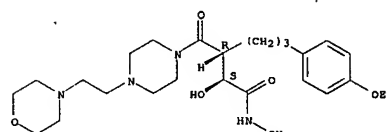
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(drug candidate; preparation of piperazine and related N-hydroxy succinic acid diamide derivs. as metalloproteinase inhibitors with therapeutic uses)

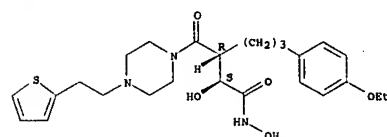
RN 874646-99-8 CAPLUS  
CN 1-Piperazinebutanamide,  $\beta$ -[3-(4-ethoxyphenyl)propyl]-N,  $\alpha$ -dihydroxy- $\gamma$ -oxo-4-[2-(4-morpholinyl)ethyl]- $\gamma$ -oxo-, (aS,BR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 874647-38-8 CAPLUS  
CN 1-Piperazinebutanamide,  $\beta$ -[3-(4-ethoxyphenyl)propyl]-N,  $\alpha$ -dihydroxy- $\gamma$ -oxo-4-[2-(2-thienyl)ethyl]-, (aS,BR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2005:162646 CAPLUS  
DOCUMENT NUMBER: 142:280227  
TITLE: Preparation of hydroxamates as matrix metalloproteinase inhibitors  
INVENTOR(S): Pain, Gilles; Davies, Stephen John; Bombrun, Agnes  
PATENT ASSIGNEE(S): Vernalis Oxford Limited, UK; Laboratoires Serono S.A.  
SOURCE: PCT Int. Appl., 89 pp.  
DOCUMENT TYPE: CODEN: PIXX02  
LANGUAGE: Patent  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION: English

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

&lt;12/04/2007&gt;

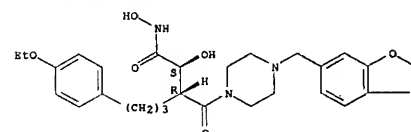
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of lymphocytes at the dose of 3 mg/kg (vs. 76% inhibition by dexamethasone at the dose of 1 mg/kg). In general, I are selective inhibitors of MMP-12 and MMP-9 relative to the collagenases and stromelysins. Therefore, I and pharmaceutical compns. thereof are useful in the treatment or prophylaxis of diseases or conditions primarily mediated by MMP-12 and/or MMP-9, especially inflammatory conditions, such as multiple sclerosis and fibrosis.

IT 847037-92-7P, (3R)-[4-[(Benzodioxol-5-yl)methyl]piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxamide  
847037-94-9P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[4-[(pyridin-4-yl)methyl]piperazin-1-yl]carbonyl]hexanoic acid hydroxamide  
847037-96-1P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[4-[(benzyl)piperazin-1-yl]carbonyl]hexanoic acid hydroxamide  
847038-26-0P, 4-[(4-Benzodioxol-5-yl)methyl]piperazin-1-yl)-(2S)-hydroxy-N-hydroxy-4-oxo-(3R)-[4-(trifluoromethoxybenzyl)butyramide  
847038-34-0P, 4-[(4-Benzodioxol-5-yl)methyl]piperazin-1-yl)-(3R)-[4-(benzyloxybenzyl)-(2S)-hydroxy-N-hydroxy-4-oxobutyramide  
847038-48-6P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[4-[(4-trifluoromethoxyphenyl)sulfonyl]piperazin-1-yl]carbonyl]hexanoic acid hydroxamide  
847038-50-0P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[4-[(4-tolylsulfonyl]piperazin-1-yl]carbonyl]hexanoic acid hydroxamide  
847038-52-2P, (3R)-[4-[(5-Bromothien-2-yl)sulfonyl]piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxamide  
847038-54-4P, (3R)-[4-[(5-Phenylsulfonylthien-2-yl)sulfonyl]piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxamide  
847038-56-6P, (3R)-[4-[(4-Butoxyphenyl)sulfonyl]piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxamide  
847038-58-8P, 6-(4-Ethoxyphenyl)-(2S)-hydroxy-(3R)-[4-[(4-methoxy-2,3,6-trimethylphenyl)sulfonyl]piperazin-1-yl]carbonyl]hexanoic acid hydroxamide  
847038-60-2P, (3R)-[4-[(3,4-Dimethoxyphenyl)sulfonyl]piperazin-1-yl]carbonyl]-6-(4-ethoxyphenyl)-(2S)-hydroxyhexanoic acid hydroxamide  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(inhibitor; preparation of hydroxamates as MMP inhibitors)  
RN 847037-92-7 CAPLUS  
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)- $\beta$ -[3-(4-ethoxyphenyl)propyl]-N,  $\alpha$ -dihydroxy- $\gamma$ -oxo-, (aS,BR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



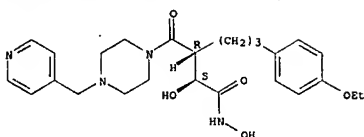
RN 847037-94-9 CAPLUS  
CN 1-Piperazinebutanamide,  $\beta$ -[3-(4-ethoxyphenyl)propyl]-N,  $\alpha$ -dihydroxy- $\gamma$ -oxo-4-(4-pyridinylmethyl)-, (aS,BR)- (9CI) (CA INDEX NAME)

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10/513699

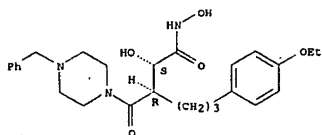
Absolute stereochemistry.



RN 847037-96-1 CAPLUS

CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-4-[(phenylmethyl)-, (αS,βR)-(9CI) (CA INDEX NAME)

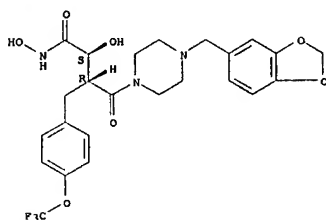
Absolute stereochemistry.



RN 847038-26-0 CAPLUS

CN 1-Piperazinebutanamide, 4-((1,3-benzodioxol-5-ylmethyl)-N, α-dihydroxy-γ-oxo-β-[(4-(trifluoromethoxy)phenyl)methyl]-, (αS,βR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 847038-34-0 CAPLUS

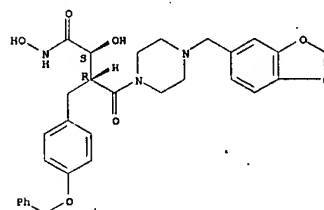
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10/513699

CN 1-Piperazinebutanamide, 4-((1,3-benzodioxol-5-ylmethyl)-N, α-dihydroxy-γ-oxo-β-[(4-(phenylmethoxy)phenyl)methyl]-, (αS,βR)-(9CI) (CA INDEX NAME)

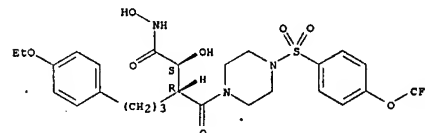
Absolute stereochemistry.



RN 847038-48-6 CAPLUS

CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-4-[(4-(trifluoromethoxy)phenyl)sulfonyl]-, (αS,βR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 847038-50-0 CAPLUS

CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-4-[(4-methylphenyl)sulfonyl]-γ-oxo-, (αS,βR)-(9CI) (CA INDEX NAME)

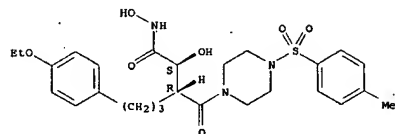
Absolute stereochemistry.



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Erich Leese

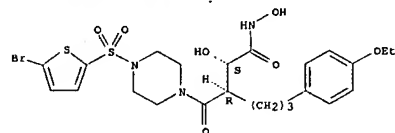
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RN 847038-52-2 CAPLUS

CN 1-Piperazinebutanamide, 4-((5-bromo-2-thienyl)sulfonyl)-β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-, (αS,βR)-(9CI) (CA INDEX NAME)

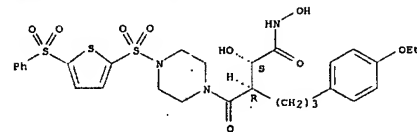
Absolute stereochemistry.



RN 847038-54-4 CAPLUS

CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-4-[(5-(phenyl)sulfonyl)-2-thienyl)sulfonyl]-, (αS,βR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



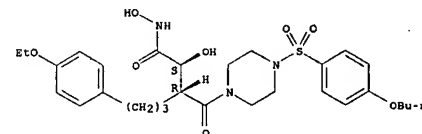
RN 847038-56-6 CAPLUS

CN 1-Piperazinebutanamide, 4-[(4-butoxyphenyl)sulfonyl]-β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-, (αS,βR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



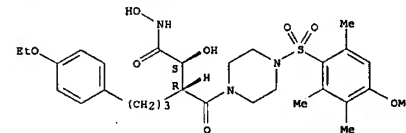
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RN 847038-58-8 CAPLUS

CN 1-Piperazinebutanamide, β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-4-[(4-methoxy-2,3,6-trimethylphenyl)sulfonyl]-γ-oxo-, (αS,βR)-(9CI) (CA INDEX NAME)

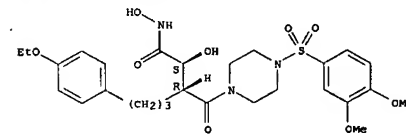
Absolute stereochemistry.



RN 847038-60-2 CAPLUS

CN 1-Piperazinebutanamide, 4-[(3,4-dimethoxyphenyl)sulfonyl]-β-[3-(4-ethoxyphenyl)propyl]-N, α-dihydroxy-γ-oxo-, (αS,βR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2003:796490 CAPLUS

DOCUMENT NUMBER: 139:307794

TITLE: Preparation of N-hydroxy (piperazinesulfonyl)- or (piperazinecarbonyl)arylpropenamides as inhibitors of histone deacetylase and antiproliferative agents for

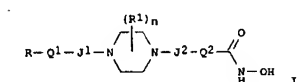
&lt;12/04/2007&gt;

Erich Leese

Instant case

INVENTOR(S): the treatment of cancer and psoriasis  
Watkins, Clare J.; Romero-Martin, Maria-Rosario;  
Ritchie, James; Finn, Paul W.; Kalvinsh, Ivars; Loza,  
Einars; Dikovska, Klara; Starchenkov, Igor; Lolya,  
Daina; Gallite, Vjia  
PATENT ASSIGNEE(S): Prolifix Limited, UK  
SOURCE: PCT Int. Appl., 217 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

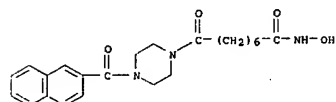
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WO 2003082288	A1	20031009	WO 2003-GB1463	20030403
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EP 1492534	A1	20050105	EP 2003-722719	20030403
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US 2005143385	A1	20050630	US 2003-509732	20030403
JP 2005527556	T	20050915	JP 2003-579825	20030403
NZ 536116	A	20070126	NZ 2003-536116	20030403
NO 2004004744	A	20041102	NO 2004-4744	20041102
PRIORITY APPL. INFO.: US 2002-369337P P 20020403				
OTHER SOURCE(S): MARPAT 139:307794				
GI				



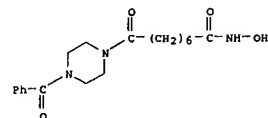
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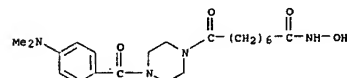
RN 610801-14-4 CAPLUS  
CN 1-Piperazineoctanamide, N-hydroxy-4-(2-naphthalenylcarbonyl)-η-oxo- (9CI) (CA INDEX NAME)



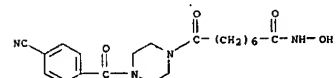
RN 610801-15-6 CAPLUS  
CN 1-Piperazineoctanamide, 4-benzoyl-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)



RN 610801-16-6 CAPLUS  
CN 1-Piperazineoctanamide, 4-[(4-(dimethylamino)benzoyl)-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)



RN 610801-17-7 CAPLUS  
CN 1-Piperazineoctanamide, 4-[(4-cyanobenzoyl)-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)



RN 610801-21-3 CAPLUS  
CN 1-Piperazineoctanamide, 4-[(4-(dimethylamino)phenylacetyl)-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)

&lt;12/04/2007&gt;

Erich Leese

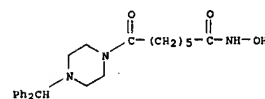
AB N-hydroxyamides I (J1 = single bond, C(=O), J2 = C(=O), SO2; Q1 = single bond, OX, SX, XOY, XSY, XO, XS; Q2 = (un)substituted C4-C8 alkylene at least four carbon atoms in length; R = (un)substituted cycloalkyl, heterocycloalkyl, or aryl; R1 = C1-C4 alkyl; X, Y = (un)substituted alkanediyl; n = 0-6) containing piperazine moieties, particularly N-hydroxy piperazinesulfonylarylpipropenamides such as II, are prepared as inhibitors of histone deacetylase (HDAC) for the treatment of proliferative diseases, cancer, and psoriasis in both humans and animals. Biol. data on the inhibition of HDAC in vitro, the inhibition of cellular proliferation in vitro, and the in vivo testing of I on mice containing i.p. P388 tumors are given for a subset of I. Most of the compds. I tested inhibit HDAC with IC50 values between 20 nM and 200 nM, inhibit proliferation of four cell lines with IC50 values between 1 μM and 10 μM, and give log rank statistics for mice with P388 tumors (5 each) of between -3 and -5. II gives a log rank statistic for tumors in five mice of -9.62. Preparative data for approx. fifty of the title compds. are given.

IT 610801-00-8P 610801-02-0P 610801-14-4P  
610801-15-5P 610801-16-6P 610801-17-7P  
610801-21-3P 610801-40-6P 610801-42-8P  
610801-43-9P 610801-44-0P 610801-46-2P  
610801-50-8P 610801-51-9P 610801-57-5P  
610801-58-6P 610801-63-3P 610801-70-2P  
610801-71-3P 610801-72-4P 610801-73-5P  
610801-76-8P

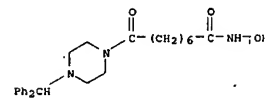
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compds.; preparation of N-hydroxy (piperazinesulfonyl)- or (piperazinecarbonyl)arylpipropenamides as inhibitors of histone deacetylase and antiproliferative agents for the treatment of cancer and psoriasis)

RN 610801-00-8 CAPLUS  
CN 1-Piperazineheptanamide, 4-(diphenylmethyl)-N-hydroxy-ζ-oxo- (9CI) (CA INDEX NAME)



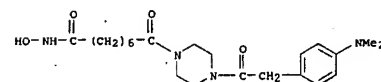
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CN 1-Piperazineoctanamide, 4-(diphenylmethyl)-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)



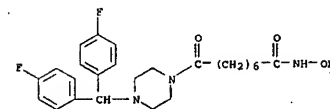
&lt;12/04/2007&gt;

Erich Leese

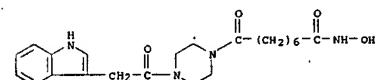
η-oxo- (9CI) (CA INDEX NAME)



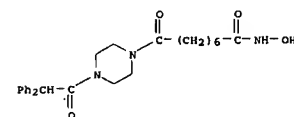
RN 610801-40-6 CAPLUS  
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RN 610801-42-8 CAPLUS  
CN 1-Piperazineoctanamide, N-hydroxy-4-(1H-indol-3-ylacetyl)-η-oxo- (9CI) (CA INDEX NAME)



RN 610801-43-9 CAPLUS  
CN 1-Piperazineoctanamide, 4-(diphenylacetyl)-N-hydroxy-η-oxo- (9CI) (CA INDEX NAME)

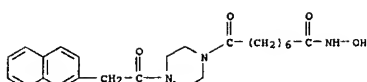


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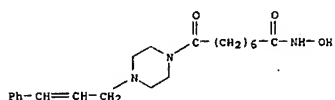
&lt;12/04/2007&gt;

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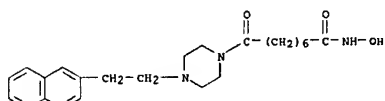
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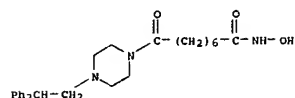
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CN 1-Piperazineoctanamide, N-hydroxy-η-oxo-4-(3-phenyl-2-propenyl)- (9CI)  
(CA INDEX NAME)



RN 610801-50-8 CAPLUS  
CN 1-Piperazineoctanamide, N-hydroxy-4-[2-(2-naphthalenyl)ethyl]-η-oxo- (9CI)  
(CA INDEX NAME)



RN 610801-51-9 CAPLUS  
CN 1-Piperazineoctanamide, N-hydroxy-4-(2,2-diphenylethyl)-η-oxo- (9CI)  
(CA INDEX NAME)

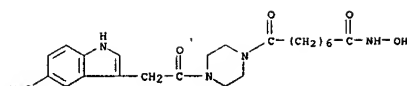


RN 610801-57-5 CAPLUS  
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(CA INDEX NAME)

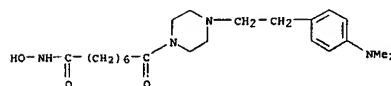
&lt;12/04/2007&gt;

Erich Leese

10/513699



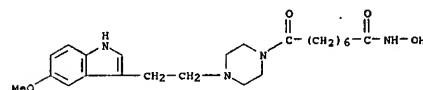
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CN 1-Piperazineoctanamide, N-hydroxy-4-[2-(4-(dimethylamino)phenyl)ethyl]-η-oxo- (9CI)  
(CA INDEX NAME)



RN 610801-63-3 CAPLUS  
CN 1-Piperazineoctanamide, N-hydroxy-4-[2-(5-methoxy-1H-indol-3-yl)ethyl]-η-oxo- (10:13) (salt) (9CI)  
(CA INDEX NAME)

CM 1

CRN 610801-62-2  
CMP C23 H34 N4 O4



CM 2

CRN 144-62-7  
CMP C2 H2 O4

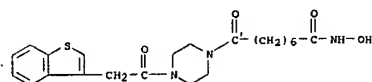


RN 610801-70-2 CAPLUS  
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(CA INDEX NAME)

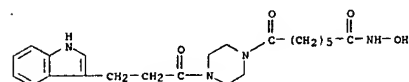
&lt;12/04/2007&gt;

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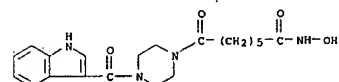
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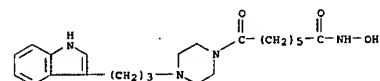
RN 610801-71-3 CAPLUS  
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(CA INDEX NAME)



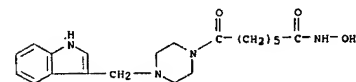
RN 610801-73-4 CAPLUS  
CN 1-Piperazineheptanamide, N-hydroxy-4-(1H-indol-3-ylcarbonyl)-η-oxo- (9CI)  
(CA INDEX NAME)



RN 610801-73-5 CAPLUS  
CN 1-Piperazineheptanamide, N-hydroxy-4-[3-(1H-indol-3-yl)propyl]-η-oxo- (9CI)  
(CA INDEX NAME)



RN 610801-76-8 CAPLUS  
CN 1-Piperazineheptanamide, N-hydroxy-4-(1H-indol-3-ylmethyl)-η-oxo- (9CI)  
(CA INDEX NAME)



&lt;12/04/2007&gt;

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10/513699

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

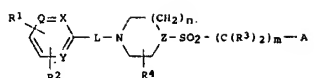
14 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2003:737742 CAPLUS  
DOCUMENT NUMBER: 139:276884  
TITLE: Preparation of sulfonyl-derivatives as novel inhibitors of histone deacetylase  
INVENTOR(S): Van Emelen, Kristof; Arts, Janine; Backx, Leo Jacobus Josef; De Winter, Hans Louis Jos; Van Brandt, Sven Franciscus Anna; Verdonck, Marc Gustaaf Celine; Meerpoel, Lieven; Pilatte, Isabelle Noelle Constance; Poncet, Virginie Sophie; Dyatkin, Alexey Borisovich; Janssen Pharmaceutica N.V., Belg.; et al.  
PATENT ASSIGNER(S): PCT Int. Appl., 139 pp.  
SOURCE: CODEN: PIXX02  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 8  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076422	A1	20030918	WO 2003-EP2516	20030311
W: AB, AO, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, OH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RN: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2476586	A1	20030918	CA 2003-2476586	20030311
AU 2003218738	A1	20030922	AU 2003-218738	20030311
EP 1485165	A1	20041215	EP 2003-711982	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007575	A	20041221	BR 2003-7575	20030311
CN 1642931	A	20050720	CN 2003-805952	20030311
JP 2005525380	T	20050825	JP 2003-574641	20030311
NZ 534830	A	20050826	NZ 2003-534830	20030311
IN 2004DN02524	A	20070413	IN 2004-DN2524	20040830
US 2005113373	A1	20050526	US 2004-507708	20040913
US 7205104	B2	20070417		
NO 2004004314	A	20041012	NO 2004-4314	20041012
US 2007142393	A1	20070621	US 2007-668096	20070130
PRIORITY APPLN. INFO.:			US 2002-163799P	P 20020313
			US 2003-120989P	P 20021024
			WO 2003-EP2516	W 20030311
			US 2004-507708	A3 20040913

OTHER SOURCE(S): MARPAT 139:276884  
01

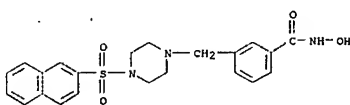
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AB This invention comprises the novel compds. (I) (wherein n = 1-3, m = 1-4, O, X, Y = N, CH; Z = N, CH; R1 = (un)substituted amido, acylamido, guanidido, and other Zn chelating group, etc.; R2 = H, halo, OH, NH2, NO2, Cl-alkyl, Cl-alkoxy, CF3, di(Cl-alkyl)amino, HOOM, naphthalenylsulfonylpiperazinyl; R3 = H aryl; R4 = H, HO, NH2, hydroxycyl-alkyl, Cl-alkyl, Cl-alkoxy, aryl(Cl-alkyl), aminocarbonyl, hydroxycarbonyl, aminoCl-alkyl, aminocarbonyl(Cl-alkyl, hydroxycarbonyl(Cl-alkyl, hydroxyaminocarbonyl, Cl-alkoxycarbonyl, Cl-alkylamino, di(Cl-alkyl)amino(Cl-alkyl; L = nul or bivalent radical selected from Cl-alkanedyl, amino, carbonyl or aminocarbonyl; A = Aryl, cyclohexyl, heterocyclic derivs.), having histone deacetylase inhibiting enzymic activity; their preparation, compns. containing them and their use as a medicine. For example, 4-(4-(2-naphthylsulfonyl)piperazin-1-yl)-N-hydroxybenzamide in 100% yield was prepared by the hydrogenation of 4-(4-(2-naphthylsulfonyl)piperazin-1-yl)-N-(phenylmethoxy)benzamide (II) in THF by Pd/C as a catalyst. II was prepared from 1,1-dimethylethyl 4-(4-carboxyphenyl)-1-piperazinecarboxylate and O-(phenylmethoxy)hydroxylamine hydrochloride in presence of dimethylaminopyridine in CH2Cl2 and diisopropylcarbodiimide, forming 1,1-dimethylethyl 4-[4-(phenylmethoxy)aminocarbonylphenyl]-1-piperazinecarboxylate which was saponified and subsequently reacted with 2-naphthalenesulfonyl chloride to give the II.

IT 604769-02-0F  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(Preparation of sulfonyl deriva. as histone deacetylase inhibitors and antitumor agent for treatment of cancer)  
RN 604769-02-0 CAPLUS  
CN Benzamide, N-hydroxy-3-[(4-(2-naphthalenylsulfonyl)-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

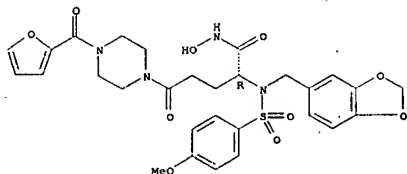


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2003:485895 CAPLUS  
DOCUMENT NUMBER: 139:233711  
TITLE: Novel inhibitors of procollagen C-Proteinase. Part 2: glutamic acid hydroxamates  
AUTHOR(S): Robinson, L. A.; Wilson, D. M.; Delset, N. G. J.;

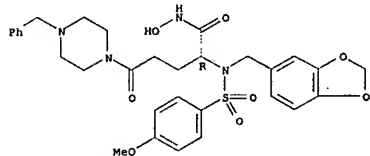
&lt;12/04/2007&gt;

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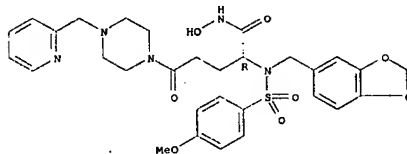
RN 591766-14-2 CAPLUS  
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-N-hydroxy-δ-oxo-4-(phenylmethyl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 591766-15-3 CAPLUS  
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-N-hydroxy-δ-oxo-4-(2-pyridinylmethyl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 591766-16-4 CAPLUS  
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-

&lt;12/04/2007&gt;

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Bradley, E. K.; Dankwardt, S. M.; Campbell, J. A.; Martin, R. L.; Van Wart, H. E.; Walker, K. A. M.; Sullivan, R. W.  
CombiChem Inc., San Diego, CA, 92121, USA  
Bioorganic & Medicinal Chemistry Letters (2003), 13(14), 2381-2384  
CODEN: BMCLEB; ISSN: 0960-894X

CORPORATE SOURCE:  
SOURCE:

PUBLISHER:  
DOCUMENT TYPE:  
LANGUAGE:  
OTHER SOURCE(S):

CASREACT 139:233711  
AB Glutamic acid derived hydroxamates were identified as potent and selective inhibitors of procollagen C-proteinase, an essential enzyme for the processing of procollagens to fibrillar collagens. Such compds. have potential therapeutic application in the treatment of fibrosis.  
IT 279255-56-0P 279255-58-2P 591766-14-2P  
591766-15-3P 591766-16-4P 591766-17-5P

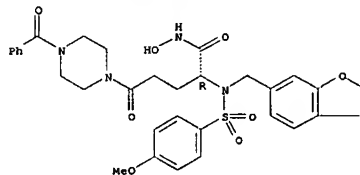
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Preparation and structure-activity relationship of glutamic acid hydroxamates as novel inhibitors of procollagen C-Proteinase)

RN 279255-56-0 CAPLUS

CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-4-benzoyl-N-hydroxy-δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 279255-58-2 CAPLUS

CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-4-(2-furanylcarbonyl)-N-hydroxy-δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

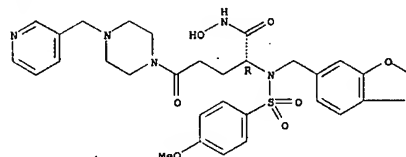
Absolute stereochemistry.

&lt;12/04/2007&gt;

Erich Leese

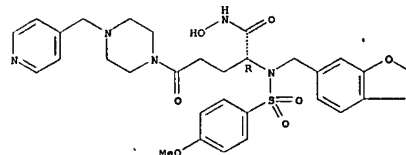
methoxyphenyl)sulfonyl]amino]-N-hydroxy-δ-oxo-4-(3-pyridinylmethyl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 591766-17-5 CAPLUS  
CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)[(4-methoxyphenyl)sulfonyl]amino]-N-hydroxy-δ-oxo-4-(4-pyridinylmethyl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2003:300644 CAPLUS  
DOCUMENT NUMBER: 138:304308  
TITLE: Preparation of sulfonyl aryl hydroxamates and their use as matrix metalloprotease inhibitors  
INVENTOR(S): Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Decrescenzo, Gary A.; Preskoe, John N.; German, Daniel P.; McDonald, Joseph Z.; Mischke, Brent V.; Rao, Shashidhar N.; Villamil, Clara I.  
PATENT ASSIGNEE(S): Pharmacia Corp., USA  
SOURCE: U.S. Pat. Appl. Publ., 148 pp., Cont.-in-part of U.S. Ser. No. 569,034.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 11

&lt;12/04/2007&gt;

Erich Leese

10/513699

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073845	A1	20030417	US 2001-909227	20010719
US 6696449	B2	20040224		
WO 9838659	A1	19980911	WO 1998-US4300	19980304
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KP, KR, LC, LR, LT, LV, MD, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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US 2001020021	A1	20010906	US 1999-230209	19990624
US 6380258	B2	20020430		
US 7115632	B1	20061003	US 2000-569034	20000511
US 2003191317	A1	20031009	US 2000-728408	20001201
US 6794511	B2	20040921		
CA 2453613	A1	20030130	CA 2002-2453613	20020719
WO 2001007954	A2	20030130	WO 2002-US23219	20020719
WO 2003007954	A3	20031023		
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RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GU, GW, ML, MR, NE, SN, TD, TG				
AU 2002326432	A1	20030303	AU 2002-326432	20020719
EP 1406626	A2	20040414	EP 2002-761148	20020719
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BR 2002011430	A	20040713	BR 2002-11430	20020719
JP 2005502632	T	20050127	JP 2003-513561	20020719
PRIORITY APPL. INFO.:				
			US 1997-35182P	P 19970304
			WO 1998-US4300	W 19980304
			US 1999-110813	B2 19990512
			US 1999-230209	A2 19990624
			US 2000-569034	A2 20000511
			US 2000-728408	A2 20001201
			US 2001-909227	A 20010719
			WO 2002-US23219	W 20020719

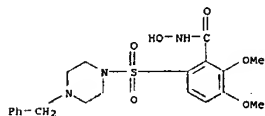
OTHER SOURCE(S): MARPAT 138:104308  
OI

&lt;12/04/2007&gt;

Erich Leece

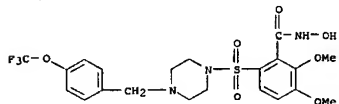
10/513699

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2003:76616 CAPLUS

DOCUMENT NUMBER: 138:117647

TITLE: Sulfonyl aryl hydroxamates and their use as matrix metalloprotease inhibitors

INVENTOR(S): McDonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Rao, Shashidhar N.; Freskos, John N.; De Crescenzo, Gary A.; Mischke, Brent V.; Getman, Daniel P.; Villamil, Clara I.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA, et al.

SOURCE: PCT Int. Appl., 214 pp.

CODEN: PIXKD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

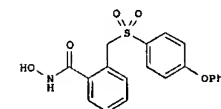
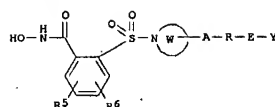
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007954	A2	20030130	WO 2002-US23219	20020719
WO 2003007954	A3	20031023		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

&lt;12/04/2007&gt;

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AB Title compds. I [W = 6-membered heterocycle containing the sulfonyl bonded N; A-R-E-Y = 4-substituent; A = O, SOO-2, etc.; R = alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, etc.; E = absent, bond, CO, SO2, etc.; Y = absent, H, OH, CH, NO2, alkyl, haloalkyl, aminoalkyl; R5-6 = together with the atoms to which they are bonded, form an aliphatic or aromatic carbocyclic

OR

heterocyclic ring having 5-7 members) are prepared. Over 50 synthetic examples are disclosed. For example, phthalide is reacted with 4-(phenoxy)benzenethiol (DMP, K2CO3, 100°C, 2 h) and the resulting product converted to the hydroxamic acid (CH2Cl2, EtOAc, DMP (cat), TMSOH, 0°C, 1.5 h) followed by oxidation (CH2Cl2, mCPBA, room temperature, 3 h) to II. II has IC50 = 10 nM for MMP-2, 45 nM for MMP-13 and >10,000 nM for MMP-1. I are inhibitors of MMP and angiogenesis.

IT

308385-85-5P 308385-86-6P 308385-87-7P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

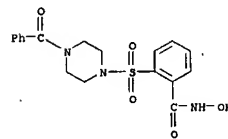
(use of sulfonyl aryl or heteroaryl hydroxamic acids and derivs. as aggrecanase inhibitors)

RN

308385-85-5 CAPLUS

CN

Benzamide, 2-[[4-(benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 308385-86-6 CAPLUS

&lt;12/04/2007&gt;

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KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GU, GW, ML, MR, NE, SN, TD, TG

US 2003073845 A1 20030417 US 2001-909227 20010719

US 6696449 B2 20040224

CA 2453613 A1 20030130 CA 2002-2453613 20020719

AU 2002326432 A1 20030303 AU 2002-326432 20020719

EP 1406626 A2 20040414 EP 2002-761148 20020719

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

BR 2002011430 A BR 2002-11430 20020719

JP 2005502632 T 20050127 JP 2003-513561 20020719

PRIORITY APPL. INFO.:

US 1997-35182P P 19970304

WO 1998-US4300 W 19980304

US 1999-110813 B2 19990512

US 1999-230209 A2 19990624

US 2000-569034 A2 20000511

US 2000-728408 A2 20001201

WO 2002-US23219 W 20020719

OTHER SOURCE(S): MARPAT 138:117647

AB The invention discloses sulfonyl aromatic hydroxamic acid compds. and salts thereof that, inter alia, inhibit matrix metalloprotease (MMP) activity and/or aggrecanase activity. The invention also is directed to a process that comprises administering such a compound or pharmaceutically acceptable salt thereof to a host animal having a condition associated with MMP activity.

IT

308385-85-5P 308385-86-6P 308385-87-7P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

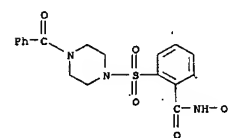
(use of sulfonyl aryl or heteroaryl hydroxamic acids and derivs. as aggrecanase inhibitors)

RN

308385-85-5 CAPLUS

CN

Benzamide, 2-[[4-(benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



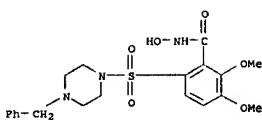
RN 308385-86-6 CAPLUS

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)

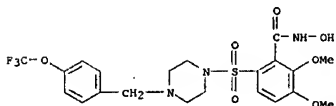
&lt;12/04/2007&gt;

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10/513699



RN 308385-87-7 CAPLUS  
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN

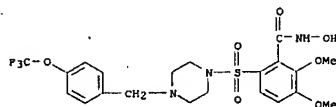
ACCESSION NUMBER: 2003:76594 CAPLUS  
DOCUMENT NUMBER: 138:117646  
TITLE: Use of sulfonyl aryl or heteroaryl hydroxamic acids and derivatives as aggregase inhibitors  
INVENTOR(S): McDonald, Joseph J.; Barta, Thomas A.; Arner, Elizabeth; Boehm, Terri L.; Becker, Daniel P.; Decrescenzo, Gary A.  
PATENT ASSIGNEE(S): Pharmacia Corporation, USA  
SOURCE: PCT Int. Appl., 274 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007930	A2	20030130	WO 2002-US22867	20020719
WO 2003007930	A3	20030821		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, JP, KE, KG, KP, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PA, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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US 2003171404	A1	20030911	US 2002-194897	20020712
US 6683078	B2	20040127		

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L4 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2003:43028 CAPLUS  
DOCUMENT NUMBER: 138:106596  
TITLE: Preparation of thiophenedicarboxamides and related compounds as histone deacetylase (HDAC) inhibitors.  
INVENTOR(S): Lesser-Reiff, Ulrike; Sattelkau, Tim; Zimmermann, Gerd  
PATENT ASSIGNEE(S): Hoffman-La Roche, Inc., Germany  
SOURCE: U.S. Pat. Appl. Publ., 19 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003013757	A1	20030116	US 2002-167677	20020611
US 6784173	B2	20040831		
CA 2449804	A1	20030213	CA 2002-2449804	20020613
WO 2003011851	A2	20030213	WO 2002-EP6488	20020613
WO 2003011851	A3	20030918		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, JP, KE, KG, KP, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PA, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IL, IN, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO				
AU 2002355626	A1	20030217	AU 2002-355626	20020613
EP 1401824	A2	20040331	EP 2002-791436	20020613
EP 1401824	B1	20061025		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1516697	A	20040728	CN 2002-812010	20020613
BR 2002010424	A	20040817	BR 2002-10424	20020613
NZ 529874	A	20041224	NZ 2002-529874	20020613
JP 2005026441	T	20050127	JP 2003-517043	20020613
AT 343569	A	20061115	AT 2002-791436	20020613
RU 2289580	C2	20061220	RU 2003-137578	20020613
ZA 2003009260	A	20050228	ZA 2003-9260	20031127
IN 2003CN01981	A	20060106	IN 2003-CN1981	20031211
BO 108450	A	20050131	BO 2003-108450	20031215
US 200424862	A1	20041028	US 2004-847166	20040537
HK 1065787	A1	20061117	HK 2004-108497	20041029
PRIORITY APPLN. INFO.:			EP 2001-114496	A 20010615

&lt;12/04/2007&gt;

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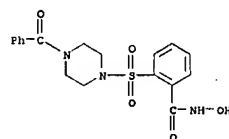
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2453602	A1	20030130	CA 2002-2453602	20020719
AU 2002327264	A1	20030303	AU 2002-327264	20020719
EP 1406602	A2	20040414	EP 2002-763298	20020719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO				
BR 2002011210	A	20040713	BR 2002-11210	20020719
JP 200504026	T	20050210	JP 2003-513538	20020719
PRIORITY APPLN. INFO.:			US 2001-306629P	P 20010719
			WO 2002-US22867	W 20020719

OTHER SOURCE(S): MARPAT 138:117646  
AB The invention discloses a process for inhibiting aggregase activity. The process comprises administering a therapeutically effective amount of a sulfonyl aromatic or heteroatom, hydroxamic acid, a derivative thereof, or a pharmaceutically acceptable salt of the hydroxamic acid or derivative to a host animal.

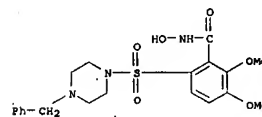
IT 308385-85-5P 308385-86-6P 308385-87-7P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(use of sulfonyl aryl or heteroaryl hydroxamic acids and derivs. as aggregase inhibitors)

RN 308385-85-5 CAPLUS  
CN Benzamide, 2-[[4-(benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



RN 308385-86-6 CAPLUS  
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-87-7 CAPLUS  
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)

&lt;12/04/2007&gt;

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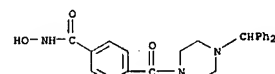
10/513699

US 2002-167677 A3 20020611  
WO 2002-EP6488 W 20020613

OTHER SOURCE(S): MARPAT 138:106596  
AB HONHCOACONR12 (A = (substituted) Ph, thienyl, R1, R2 = H, (substituted) alkyl, carbocyclyl, heterocyclyl; NR1R2 = (substituted) 3-6 membered ring), were prepared. Thus, thiophene-2,5-dicarboxylic acid monomethyl ester and N-methylmorpholine in CH2Cl2 at -10° were treated with 1-aminomethylphenylthiophene in CH2Cl2; the mixture was stirred 90 min to give 5H monomide. This was stirred with NH2OH.HCl and NaOMe in MeOH for 4 h to give thiophene-2,5-dicarboxylic acid 2-hydroxyamide 5-[(naphthalen-1-ylmethyl)amide]. Tested title compds. inhibited HT-29 tumor cell growth with IC50 = 0.02-0.17 µM. A tablet formulation is given.

IT 487004-50-2P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(claimed compound; preparation of thiophenedicarboxamides and related compds. as histone deacetylase (HDAC) inhibitors)

RN 487004-50-2 CAPLUS  
CN Benzamide, 4-[[4-(diphenylmethyl)-1-piperazinyl]carbonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2002:119307 CAPLUS  
DOCUMENT NUMBER: 137:75137  
TITLE: Predictions of Binding of a Diverse Set of Ligands to Gelatinase-A by a Combination of Molecular Dynamics and Continuum Solvent Models  
AUTHOR(S): Hou, Tingjun; Guo, Senli; Xu, Xiaojie  
CORPORATE SOURCE: College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China  
SOURCE: Journal of Physical Chemistry B (2002), 106(21), 5527-5535  
CODEN: JPCBPK; ISSN: 1089-5647  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The free energies of binding, ΔGbind, between a diverse set of eight hydroxamate inhibitors with gelatinase-A (MMP-2) were computed by using the recently developed MM/PBSA approach. In this paper, a nonbonded model was used to represent the potentials of the catalytic zinc center. Mol. dynamics (MD) simulations were used to generate the thermally averaged ensemble of conformations of the ligand-protein complexes. On the basis of the trajectories from MD simulations, the free energies of binding were calculated using mol. mechanics, the continuum solvent model, surface area

&lt;12/04/2007&gt;

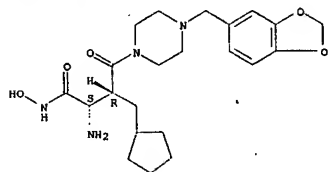
Erich Leese

estimation, and normal-mode anal. The results show that MM/PBSA not only can rank the studied ligands effectively but also can reproduce the exptl. binding free energies successfully. The predicted binding free energies correlate well with the exptl. values ( $r = 0.84$ ,  $q = 0.78$ ). As a comparison, the free energies of binding were also computed by using the linear interaction energy approximation (LIE). The overall agreement between the calculated and exptl. values for the diverse set of ligands means that the MM/PBSA approach is a useful tool for the general evaluation of protein-ligand interactions. The anal. of the sep. energy terms contributing to MM/PBSA free energy indicates that the association between hydroxamate and MMP-2 is mainly driven by more favorable van der Waals/nonpolar interactions in the complex than in solution

IT 220046-45-7  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (linear interaction energy approximation reveals association between hydroxamate and MMP-2 is promoted by van der Waals/nonpolar interactions in complex than in solution)

RN 220046-45-7 CAPLUS  
CN 1-Piperazinebutanamide,  $\alpha$ -amino-4-(1,3-benzodioxol-5-ylmethyl)- $\beta$ -(cyclopentylmethyl)-N-hydroxy- $\gamma$ -oxo-, (as, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



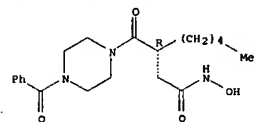
REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2002:275960 CAPLUS  
DOCUMENT NUMBER: 136:310184  
TITLE: Preparation of hydroxamic acid peptide deformylase inhibitors as antibacterial agents  
INVENTOR(S): Chong, Lee; Frechette, Roger; Scott, Carole; Tester, Richard; Smith, Whitney; Chiba, Katsumi; Sakamoto, Masatoshi; Gluchowski, Charles  
PATENT ASSIGNEE(S): Questcor Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 171 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

<12/04/2007>

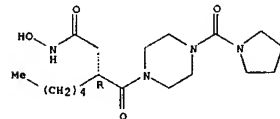
Erich Leese

Absolute stereochemistry.



RN 409129-96-0 CAPLUS  
CN 1-Piperazinebutanamide, N-hydroxy- $\gamma$ -oxo- $\beta$ -pentyl-4-(1-pyrrolidinylcarbonyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2002:161702 CAPLUS  
DOCUMENT NUMBER: 137:5788  
TITLE: Binding free energy calculations for MMP2-hydroxamate complexes  
AUTHOR(S): Hou, Ting-Jun; Zhang, Wei; Xu, Xiao-Jie  
CORPORATE SOURCE: College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China  
SOURCE: Huaxue Xuebao (2002), 60(2), 221-227  
CODEN: HHNPA4, ISSN: 0567-7351  
PUBLISHER: Kexue Chubanshe  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese

AB The absolute binding affinities of hydroxamate inhibitors with MMP-2 were evaluated by mol. dynamics (MD) simulations with a linear response approach. During MD simulations, a nonbonded model for the catalytic Zn center was used to represent the interactions between Zn center and enzyme/inhibitor. The trajectories from MD simulation show that using the nonbonded model the catalytic Zn ion adopts five coordination number, but the coordination form exists large difference with that of the initial model. After fittings, the models with one parameter, two parameters and three parameters were obtained. The calculated results indicate that the three-parameter model with a constant term bears the best predicting ability. The best model yields an average error of 2.38 kJ/mol for the eight binding affinities of hydroxamates.

IT 220046-45-7  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

<12/04/2007>

Erich Leese

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028829	A2	20020411	WO 2001-US29926	20010924
WO 2002028829	A3	20031224		
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
KM: GH, GM, KE, LS, MM, ME, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, OA, OR, QZ, GW, ML, MR, NE, SN, TD, TG				
AU 2002030385	A5	20020415	AU 2002-30385	20010924
PRIORITY APPLN. INFO.:			US 2000-234967P	P 20000925
			US 2001-761850	A 20010118
			WO 2001-US29926	N 20010924

OTHER SOURCE(S): MARPAT 136:310184  
OI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Hydroxamic acid derivs. of peptides and peptidomimetics of formulas I, II, and III [wherein Z = NHOH or ORa; Ra = alkyl or a biocleavable moiety; X = CO or SO<sub>2</sub>; Y = (un)substituted heteroalkyl or heterocyclyl; R<sub>1</sub> = (un)substituted (cyclo)alkyl, aryl, heterocyclyl, or heteroalkyl; R<sub>2</sub>R<sub>3</sub> = 4-7 membered (un)substituted heterocycle; R<sub>2</sub>R<sub>4</sub> = ring formed through a CH<sub>2</sub>CH<sub>2</sub> linkage; or R<sub>2</sub> = Me; or R<sub>3</sub> = H or (un)substituted (hetero)alkyl, aryl, or heterocyclyl; or R<sub>4</sub> = H or (un)substituted (hetero)alkyl, aryl, or heterocyclyl; R<sub>5</sub> and R<sub>6</sub> = independently H, NO<sub>2</sub>, NH<sub>2</sub>, NHC(=O)H, NHC(=O)CH<sub>3</sub>, NHC(=O)CH<sub>2</sub>CH<sub>3</sub>, or (un)substituted CH<sub>2</sub>NH-(hetero)alkyl or CH<sub>2</sub>NH-heterocyclyl; one of R<sub>7</sub> or R<sub>8</sub> = CH<sub>2</sub>CONH(OR<sub>9</sub>); one of R<sub>7</sub> or R<sub>8</sub> = (un)substituted (hetero)alkyl, (alkyl)heterocyclyl, or alkylaryl; R<sub>9</sub> and R<sub>10</sub> = independently H or (un)substituted (hetero)alkyl, (alkyl)heterocyclyl, or alkylaryl] were prepared as peptide deformylase (Pe-PDF) inhibitors for treating various bacterial infections. For example, 3-pyrrolidinol was added to tert-Bu (R)- (2-pentyl)succinate mono(N-hydroxysuccinimide) ester to give the amide (68b). Treatment with 20% TFA/DCM, followed by MeOH, benzene, and THMSH in hexane, afforded the Me ester (90a). The pyrrolidinol was coupled with 4-methoxyphenylisocyanate and the ester converted to the hydroxamic acid (IV) using NH<sub>2</sub>OH·HCl. The latter inhibited E. coli Pe-PDF with IC<sub>50</sub> of 9 nM and showed selectivity for Pe-PDF vs. thermolysin with a selectivity index of 30,000. Thus, I, II, and III are useful as antibiotics against a broad range of infectious disease in animals and humans.

IT 409129-95-9 CAPLUS  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(peptide deformylase inhibitor; preparation of hydroxamic acid derivs. of peptides and peptidomimetics as peptide deformylase inhibitors for treatment of infectious diseases)

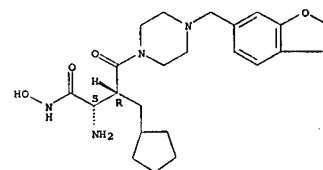
RN 409129-95-9 CAPLUS  
CN 1-Piperazinebutanamide, 4-benzoyl-N-hydroxy- $\gamma$ -oxo- $\beta$ -pentyl-, (R)- (9CI) (CA INDEX NAME)

<12/04/2007>

Erich Leese

(Biological study)  
(binding free energy calcns. for MMP2-hydroxamate complexes)  
RN 220046-45-7 CAPLUS  
CN 1-Piperazinebutanamide,  $\alpha$ -amino-4-(1,3-benzodioxol-5-ylmethyl)- $\beta$ -(cyclopentylmethyl)-N-hydroxy- $\gamma$ -oxo-, (as, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 2001:433270 CAPLUS  
DOCUMENT NUMBER: 135:371526  
TITLE: Preparation of sulfonyl aryl or heteroaryl hydroxamic acid compounds as inhibitors of matrix metalloproteinase  
INVENTOR(S): Bedell, Louis J.; Mcnald, Joseph; Barta, Thomas E.; Becker, Daniel P.; Rao, Shashidhar N.; Preskott, John W.; Mischke, Brent V.; Gutman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.  
PATENT ASSIGNEE(S): Pharmacia Corporation, USA  
SOURCE: PCT Int. Appl., 374 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 11  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085680	A2	20011115	WO 2001-US14706	20010507
WO 2001085680	A3	20020307		
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
KM: GH, GM, KE, LS, MM, ME, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, OA, ON, OW, ML, MR, NE, SN, TD, TG				
US 7115633	B1	20061003	US 2000-569034	20000511
PRIORITY APPLN. INFO.:			US 2000-569034	A 20000511
			US 1999-310813	B2 19990512

<12/04/2007>

Erich Leese

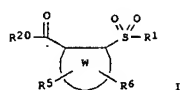
10/513699

OTHER SOURCE(S):  
GI

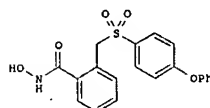
MARPAT 135:371526

US 1999-230209

A2 19990624



I



II

AB Title compds. I [W = 5-, 6-membered aromatic or heteroarom. ring; R1 = a substituent containing a 5- or 6-membered cyclohydrocarbyl, heterocyclo, aryl, or heteroaryl radical that is bonded directly to the depicted SO<sub>2</sub>-group said R1 with certain steric requirements; R5-6 = H, alkyl, cycloalkyl, acylalkyl, halo, nitro, hydroxy, cyano, alkoxy, haloalkyl, haloalkoxy, hydroxyalkyl, etc. or R5-6 together with the atoms to which they are bonded form a further aliphatic or aromatic carbocyclic or heterocyclic ring having 5-to 7-members; R20 = OR21, where R21 = H, alkyl, aryl, arylalkyl, NR13OR22, where R22 = a selectively removable protecting group and R13 = H, alkyl, benzyl group, etc.] were prepared Over 50 synthetic examples were disclosed. For example, phthalide was reacted with 4-(phenoxy)benzenethiol (DMP, K<sub>2</sub>CO<sub>3</sub>, 100°C, 2 h) and the resulting product converted to the hydroxamic acid (CH<sub>2</sub>Cl<sub>2</sub>, ClCOCOCl, DMP (cat), TMSOH, 0°C, 1.5 h) followed by oxidation (CH<sub>2</sub>Cl<sub>2</sub>, MCPBA, room temperature, 3 h) to II. II had IC<sub>50</sub> = 10 nM for MMP-2, 45 nM for MMP-13 and >10,000 nM for MMP-1. I are inhibitors of MMP and angiogenesis.

IT 308385-85-SP, 2-[(4-Benzoyl-1-piperazinyl)sulfonyl]-N-hydroxybenzamide 373367-17-0P, N-Hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl)sulfonyl]benzamide hydrochloride 373367-18-1P, N-Hydroxy-2,3-dimethoxy-6-[[4-[(4-(trifluoromethoxy)phenyl)methyl]-1-piperazinyl)sulfonyl]benzamide hydrochloride

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as inhibitors of matrix metalloproteinase)

RN 308385-85-5 CAPLUS

CN Benzamide, 2-[(4-benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)

&lt;12/04/2007&gt;

Erich Leese

10/513699

PATENT ASSIGNEE(S):  
SOURCE:

Marie-agnes; Moureau, Florence; Ryckmans, Thomas; Taverne, Thierry; Henichart, Jean-pierre; Neuvels, Michel; Goldstein, Solo Ucb, S.A., Belg.

DOCUMENT TYPE:  
LANGUAGE:

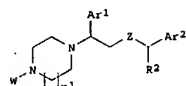
PCT Int. Appl., 115 pp.  
CODEN: PIXXD2  
Patent  
English

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046167	A1	20010628	WO 2000-EP12667	20001214
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, EG, FI, FR, GB, GD, GE, GR, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NZ, NI, NO, NU, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KO, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, BG, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CP, CO, CI, CM, GA, GM, GW, ML, MR, NE, SN, TD, TG				
EP 1110958	A1	20010627	EP 1999-125359	19991220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1242399	A1	20020925	EP 2000-989974	20001214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518108	T	20030603	JP 2001-547078	20001214
US 2003220323	A1	20031127	US 2002-168331	20020830
US 6916797	B2	20050712		
PRIORITY APPLN. INFO.: EP 1999-125359 A 19991220 WO 2000-EP12667 W 20001214				

OTHER SOURCE(S):  
GI

MARPAT 135:61355



I

AB The title compds. I [Z = O, S; n1 = 1-2; R2 = H, Me; W = cyclohexyl substituted by a CO<sub>2</sub>H, 2-phenylacetic acid, or alkyl 2-phenylacetate, etc.; Ar1 = (un)substituted Ph, aryl, heteroaryl, etc.; Ar2 = (un)substituted Ph, etc.] and their salts, useful as neurokinin receptor antagonists (NK1antagonists), were prepared Thus, hydrolysis of the corresponding Et ester afforded I [Z = O; R2 = H; n1 = 1; W = (CH<sub>2</sub>)<sub>4</sub>CO<sub>2</sub>H; Ar1 = Ph; Ar2 = 3,5-(F<sub>3</sub>C)<sub>2</sub>CH<sub>3</sub>] which showed pIC<sub>50</sub> of 7.5 against binding to NK1 receptors. The compds. I are useful for the prevention and/or treatment of a condition associated with pathol. levels of substance P.

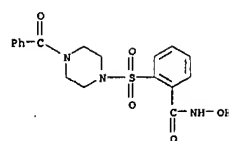
IT 346416-43-1P 346416-44-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

&lt;12/04/2007&gt;

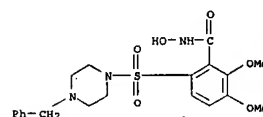
Erich Leese

10/513699



RN 373367-17-0 CAPLUS

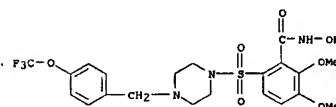
CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl)sulfonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 373367-18-1 CAPLUS

CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[(4-(trifluoromethoxy)phenyl)methyl]-1-piperazinyl)sulfonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:472692 CAPLUS

DOCUMENT NUMBER: 135:61355

TITLE: Preparation of α-arylethylpiperazine derivatives as neurokinin antagonists

INVENTOR(S): Stiernet, Francoise; Genicot, Christophe; Lasseo,

&lt;12/04/2007&gt;

Erich Leese

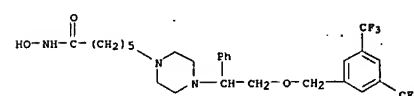
10/513699

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of α-arylethylpiperazine derivs. as neurokinin antagonists)

RN 346416-43-1 CAPLUS

CN 1-Piperazinehexanamide, 4-[2-[[3,5-bis(trifluoromethyl)phenyl]methoxy]-1-phenylethyl]-N-hydroxy- (9CI) (CA INDEX NAME)



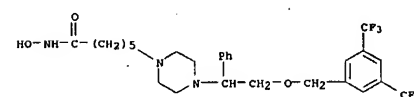
RN 346416-44-2 CAPLUS

CN 1-Piperazinehexanamide, 4-[2-[[3,5-bis(trifluoromethyl)phenyl]methoxy]-1-phenylethyl]-N-hydroxy-, (2Z)-2-butenedioate (1:2) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 346416-43-1

CMF C27 H33 F6 N3 O3

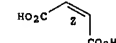


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:390470 CAPLUS

DOCUMENT NUMBER: 135:104175

TITLE: Binding Affinities for a Series of Selective

&lt;12/04/2007&gt;

Erich Leese

10/513699

Inhibitors of Gelatinase-A Using Molecular Dynamics with a Linear Interaction Energy Approach  
 Hou, T. J.; Zhang, W.; Xu, X. J.  
 College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China  
 Journal of Physical Chemistry B (2001), 105(22), 5304-5315  
 CODEN: JPCBFX; ISSN: 1069-5647  
 American Chemical Society  
 PUBLISHER:  
 DOCUMENT TYPE:  
 LANGUAGE:  
 AB The binding of a series of hydroxamate inhibitors with gelatinase-A is examined to evaluate the viability of calculating free energies of binding. AGB, utilizing mol. dynamics (MD) simulations with a linear interaction energy approach. In our simulations, a bonded model was used to represent the potentials of the catalytic zinc center. The electrostatic distribution of this model was derived using a two-stage electrostatic potential fitting calcs. The resulting bonded model was then used to generate the MD trajectories. Coulombic, van der Waals, and coordinate bond energy components determined from MD simulations of the bound and unbound inhibitors solvated in water were correlated with the free energies of binding for the 15 hydroxamate inhibitors. In the correlation process, several linear models consisted of different energy components were tested. We found that besides the usually used Coulombic and van der Waals energy terms, the introduction of a constant term could significantly improve the correlation. The best model yields an average error of 0.6 kcal/mol for the 15 binding affinities, which cover an observed range of 7.2 kcal/mol. The predictive ability of the best model was revealed by the high value of q2 (0.85) from the leave-one-out cross-validation. To this series of inhibitors, the constant term can be treated as effective adjustment to the entropy contribution in the binding free energies. The MD simulations predicted the binding mode of the gelatinase-A with the studied inhibitors, and also provided insights into the interactions occurring in the active site and the origins of variations in AGB. The P1' groups of inhibitors make extensive van der Waals and hydrophobic contacts with the nonpolar side chains of four residues in the S1' subsite, including Leu 197, Val 198, Leu 218, and Tyr 223, which directly influence the ligand binding. Hydrogen bonds between hydroxamates and gelatinase-A are very important to stabilize the inhibitors in the active site. The hydrogen bonds between the P3' group and gelatinase-A can produce more favorable electrostatic interactions.

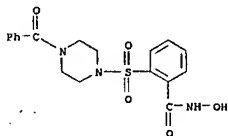
IT 220046-45-7  
 RL: BPR (Biological process), BSU (Biological study, unclassified), PRP (Properties), BIOL (Biological study), PROC (Process)  
 (binding affinities for a series of selective inhibitors of gelatinase-A using mol. dynamics with a linear interaction energy approach)  
 RN 220046-45-7 CAPLUS  
 CN 1-Piperazinebutanamide, 4-amino-4-(1,3-benzodioxol-5-ylmethyl)-[P-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, (aS, BR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

&lt;12/04/2007&gt;

Erich Leese

10/513699



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

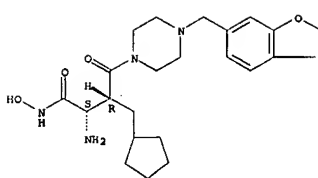
L4 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2000:824218 CAPLUS  
 DOCUMENT NUMBER: 134:4752  
 TITLE: Preparation of hydroxamic acid derivatives as matrix metalloprotease inhibitors  
 INVENTOR(S): Bedell, Louis J.; McDonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Rao, Shashidhar N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.  
 PATENT ASSIGNEE(S): G.D. Searle and Co., USA  
 SOURCE: PCT Int. Appl., 380 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 11  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069819	A1	20001123	WO 2000-US6713	20000512
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MU, MW, MY, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TT, TZ, UA, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2373500	A1	20001123	CA 2000-2373500	20000512
EP 1171713	A1	20020206	EP 2000-931910	20000512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000011291	A	20020514	BR 2000-11291	20000512
JP 2002544257	T	20021224	JP 2000-618236	20000512
NZ 515197	A	20040326	NZ 2000-515197	20000512
AU 781339	B2	20050519	AU 2000-49718	20000512
ZA 2001009007	A	20030131	ZA 2001-9007	20011031
PRIORITY APPLN. INFO.:			US 1999-310813	A 19990512
			WO 2000-US6713	W 20000512
OTHER SOURCE(S):			MARPAT 134:4752	
GI				

&lt;12/04/2007&gt;

Erich Leese

10/513699



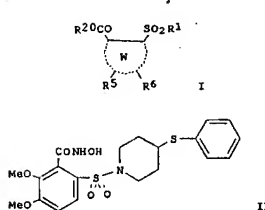
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2000:853658 CAPLUS  
 DOCUMENT NUMBER: 134:222499  
 TITLE: Synthesis and activity of selective MMP inhibitors with an aryl backbone  
 AUTHOR(S): Barta, T. E.; Becker, D. P.; Bedell, L. J.; De Crescenzo, G. A.; McDonald, J. J.; Munie, G. E.; Rao, S.; Shieh, H.-S.; Stegeman, R.; Stevens, A. M.; Villamil, C. I.  
 CORPORATE SOURCE: Pharmacia, Department of Medicinal Chemistry, Skokie, IL, 60077, USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(24), 2815-2817  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 134:222499  
 AB A series of novel, MMP-1 sparing arylhydroxamate sulfonamides with activity against MMP-2 and MMP-13 is described. Example compds. thus tested were N-hydroxy-2-[[4-(phenylmethyl)amino]sulfonyl]benzamide, N-hydroxy-2-[[4-(methoxyphenyl)methylamino]sulfonyl]benzamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]benzamide, 2-fluoro-N-hydroxy-6-[[4-(4-(trifluoromethyl)phenoxy)-1-piperidinyl]sulfonyl]benzamide, and derivs. or homologs thereof. The crystal and mol. structure of 2-fluoro-N-hydroxy-6-[[4-(4-(trifluoromethyl)phenoxy)-1-piperidinyl]sulfonyl]benzamide compound with MMP-8 were reported.  
 IT 308385-85-5  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (aminosulfonyl)-N-hydroxybenzamide derivs. and their activity as gelatinase (MMP-2) and collagenase (MMP-13) inhibitors  
 RN 308385-85-5 CAPLUS  
 CN Benzamide, 2-[[4-(benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)

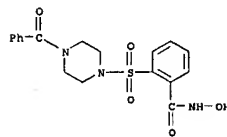
&lt;12/04/2007&gt;

Erich Leese

10/513699



AB Title compds. [I; W = 5, 6 membered aromatic, heterosom. ring; R = 5, 6 membered cyclohydrocarbyl, heterocyclic, aryl, heteroaryl; R5, R6 independently = hydro, alkyl, cycloalkyl, acylalkyl, halo, nitro, hydroxyl, cyano, alkoxy, haloalkoxy, haloalkoxy, hydroxyalkyl, etc; R20 = alkoxy, aryloxy, alkoxyamino, benzyloxyamino, etc] and pharmaceutically acceptable salts with inter alia inhibits matrix metalloprotease activity are disclosed and a treatment that comprises administering a contemplated sulfonyl aromatic or heterosom. hydroxamic acid in an MMP enzyme-inhibiting effective amount to a host having a condition associated with pathol. matrix metalloprotease activity are claimed. Thus, the title compound II was prepared and MMP-2, MMP-3, MMP-8, MMP-13, and MT1-MMP inhibition activities were assayed.  
 IT 308385-85-6P 308385-86-6P 308385-87-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPW (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of hydroxamic acid derivs. as matrix metalloprotease inhibitors)  
 RN 308385-85-5 CAPLUS  
 CN Benzamide, 2-[[4-(benzoyl-1-piperazinyl)sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)

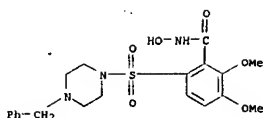


RN 308385-86-6 CAPLUS  
 CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)

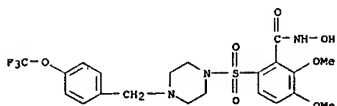
&lt;12/04/2007&gt;

Erich Leese

10/513699



RN 308385-87-7 CAPLUS  
 CN Benzamide, N-hydroxy-2,3-dimethoxy-6-[[4-[[4-(trifluoromethoxy)phenyl]methyl]-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2000:441768 CAPLUS

DOCUMENT NUMBER: 133:74324

TITLE: Preparation of amino acid sulfonamide hydroxamates as

inhibitors of procollagen C-proteinase.

INVENTOR(S): Billedeau, Roland Joseph; Broka, Chris Allen;

Campbell, Jeffrey Allen; Chen, Jian Jeffrey;

Dankwardt, Sharon Marie; Delaet, Nancy; Robinson,

Leslie Ann; Walker, Keith Adrian Murray

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 133 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

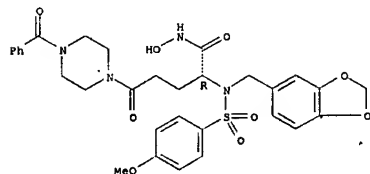
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017436	A1	20000629	WO 1999-EP9920	19991214
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW, GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GH, GW, ML, MR, NE, SN, TD, TO				
CA 2355902	A1	20000629	CA 1999-2355902	19991214
BR 9916504	A	20010911	BR 1999-16504	19991214

&lt;12/04/2007&gt;

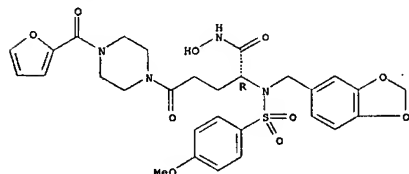
Erich Leese

10/513699



RN 279255-56-2 CAPLUS  
 CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)][4-methoxyphenyl]sulfonyl]amino]-4-(2-furanylcarbonyl)-N-hydroxy- δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 2000:161258 CAPLUS

DOCUMENT NUMBER: 132:207849

TITLE: Preparation of arylpiperazines as metalloproteinase

inhibiting agents (MMP)

INVENTOR(S): Barlaam, Bernard Christophe; Newcombe, Nicholas John;

Tucker, Howard; Waterson, David

PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca-Pharma Sa

SOURCE: PCT Int. Appl., 82 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012478	A1	20000309	WO 1999-GB2801	19990825
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,				

&lt;12/04/2007&gt;

Erich Leese

10/513699

EP 1149072	A1	20011031	EP 1999-963530	19991214
EP 1149072	B1	20040630		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101868	T2	20011121	TR 2001-200101868	19991214
HU 200104658	A2	20020629	HU 2001-4658	19991214
JP 2002533322	T	20021008	JP 2000-589508	19991214
AU 769319	B2	20040122	AU 2000-19792	19991214
NZ 512292	A	20040326	NZ 1999-512292	19991214
AT 270271	T	20040715	AT 1999-963530	19991214
RU 2232781	C2	20040720	RU 2001-119461	19991214
US 6492194	B1	20021120	US 1999-469660	19991214
HR 2001000443	A1	20020630	HR 2001-443	20010614
ZA 2001005014	A	20020919	ZA 2001-5014	20010619
MX 2001PA06328	A	20010910	MX 2001-PA6328	20010620
IN 2001CN00859	A	20050304	IN 2001-CN859	20010620
NO 2001003100	A	20010821	NO 2001-3100	20010621
US 2003199520	A1	20031023	US 2002-267292	20021009
US 6844366	B2	20050118		
US 2003216405	A1	20031120	US 2002-267727	20021009
US 6787559	B2	20040907		

PRIORITY APPLN. INFO.:

US 1998-113311P	P	19981222
US 1999-147053P	P	19990803
US 1999-164138P	P	19991108
WO 1999-EP9920	N	19991214
US 1999-469660	A3	19991222

OTHER SOURCE(S):

MARPAT 133:74324

AB HOHNOCCHRINRSO2Ar2 (R1 = alkyl, haloalkyl, heteroalkyl, cycloalkyl, aryl, aralkyl, aralkenyl, heteroaryl, heteroalkenyl, aminyl, aryl, aralkyl, etc.; R = CHR2Ar1, CHR2CH:CHAr1; Ar2 = specified (substituted) Ph, naphthyl, R2 = H, alkyl, with proviso), were prepared. Thus, N-hydroxy-2(R)-[(3,4-methylenedioxybenzyl)(4-methoxy-2,3,6-trimethylbenzenesulfonyl)amino]-3-methylbutyramide was prepared by solution phase synthesis from BOC-D-Val-OH. Title compds. inhibited procollagen C-proteinase with IC50 0.01-2 μM.

IT 279255-56-OP 279255-58-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPW (Synthetic preparation); THU (Therapeutic use); BLOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of amino acid sulfonamide hydroxamates as inhibitors of procollagen C-proteinase)

RN 279255-56-0 CAPLUS  
 CN 1-Piperazinepentanamide, α-[(1,3-benzodioxol-5-ylmethyl)][4-methoxyphenyl]sulfonyl]amino]-4-benzoyl-N-hydroxy- δ-oxo-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

&lt;12/04/2007&gt;

Erich Leese

10/513699

CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, VE, VN, YU, ZA, ZW				
RW, GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TO				

CA 2339761	A1	20000309	CA 1999-2339761	19990825
AU 9955247	A	20000321	AU 1999-55247	19990825
AU 764367	B2	20030814		
BR 9913255	A	20010522	BR 1999-13255	19990825
EP 1109787	A1	20010627	EP 1999-941751	19990825
EP 1109787	B1	20060517		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
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TR 200100605	T2	20010821	TR 2001-200100605	19990825
HU 200103344	A2	20020228	HU 2001-3344	19990825
EE 200100106	A	20020617	EE 2001-106	19990825
JP 2002523493	T	20020730	JP 2000-567511	19990825
NZ 509730	A	20030530	NZ 1999-509730	19990825
RU 2220967	C2	20040110	RU 2001-108591	19990825
NZ 524921	A	20041029	NZ 1999-524921	19990825
AT 326448	T	20060615	AT 1999-941751	19990825
PT 1109787	T	20060929	PT 1999-941751	19990825
ES 2263284	T3	20061201	ES 1999-941751	19990825
TW 240722	B	20051001	TW 1999-48114833	19990830
ZA 2001001231	A	20020513	ZA 2001-1231	20010213
MX 2001PA01847	A	20020408	MX 2001-PA1847	20010220
US 6734184	B1	20040511	US 2001-763709	20010226
NO 2001001023	A	20010425	NO 2001-1023	20010228
NO 321478	B1	20060515		
BG 105369	A	20011231	BG 2001-105369	20010322
HK 1036060	A1	20061027	HK 2001-106732	20010924
AU 2003262101	A1	20031218	AU 2001-262101	20031112
US 2004171641	A1	20040902	US 2004-787775	20040226

PRIORITY APPLN. INFO.:

OTHER SOURCE(S):

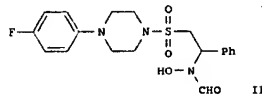
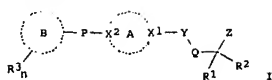
MARPAT 132:207849

GI

EP 1998-402144	A	19980831
EP 1999-401351	A	19990604
WO 1999-082801	M	19990825
US 2001-763709	A1	20010226

&lt;12/04/2007&gt;

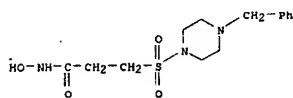
Erich Leese



AB The title compds. [I; B = monocyclic or bicyclic alkyl, aryl, etc.; R3 = H, halo, NO2, etc.; n = 1-3; P = (CH2)n (wherein n = 0-2), alkene, alkyne, etc.; A = (un)substituted 5-7 membered aliphatic ring; X1, X2 = N, C, where a ring substituent on ring A is a oxo group that is preferably adjacent a ring N atom; Y = SO2, CO; Z = CONHOH, Y = CO and Q = CR6R7, CR6R7CH2, NR6, NR6CH2 (wherein R6 = H, alkyl, aralkyl, etc.; R7 = H, alkyl; R7 together with R6 forms a carbocyclic or heterocyclic spiro 5-7 membered ring, the latter containing at least one heteroatom selected from N, O, S); Z = CONHOH, Y = SO2 and Q = CR6R7, CR6R7CH2; Z = N(OH)CHO and Q = CHR6, CHR6CH2, NR6CH2; R1 = H, alkyl, cycloalkyl, etc.; R2 = H, alkyl, aryl, etc.], useful as metalloproteinase inhibitors (no data), especially as inhibitors of MMP 13, in treating arthritis and atherosclerosis, were prepared E.g., a multi-step synthesis of the title piperazine II was given. Comps. I are effective at 0.5-30 mg/kg/day.

IT 260438-45-7P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of arylpiperazines as metalloproteinase inhibiting agents (MMPs))

RN 260438-45-7 CAPLUS  
CN Propanamide, N-hydroxy-3-[[4-(phenylmethyl)-1-piperazinyl]sulfonyl]- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN  
ACCESSION NUMBER: 1999:64787 CAPLUS  
DOCUMENT NUMBER: 130:139360

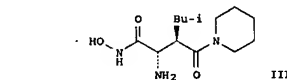
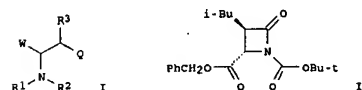
&lt;12/04/2007&gt;

Erich Leese

TITLE: Preparation of succinyl piperidinamides, morpholinamides, piperazinamides, and analogs as matrix metalloproteinase inhibitors  
INVENTOR(S): Alpegiani, Marco; Bissolino, Pierluigi; Abrate, Francesca; Perrone, Ettore; Corigli, Riccardo; Jabes, Daniela  
PATENT ASSIGNEE(S): Pharmacia & Upjohn S.P.A., Italy  
SOURCE: PCT Int. Appl., 81 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902510	A1	19990121	WO 1998-EP4220	19980707
W: AL, AU, BR, CA, CN, CZ, HU, ID, IL, JP, KR, MX, NO, NZ, PL, RO, UA, US, AM, AZ, BY, KO, KE, MD, RU, TJ, TW				
RN: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2265671	A1	19990121	CA 1998-2265671	19980707
AU 9888583	A	19990208	AU 1998-888583	19980707
EP 925289	A1	19990630	EP 1998-940170	19980707
R: DE, ES, FR, GB, IT, SE				
JP 2001500533	T	20010116	JP 1999-508146	19980707
US 6482827	B1	20021119	US 1999-147798	19990310
PRIORITY APPLN. INFO.:			GB 1997-14548	A 19970710
			GB 1997-24395	A 19971118
			WO 1998-EP4220	M 19980707

OTHER SOURCE(S): MARPAT 130:139360  
GI



AB Title compds. I (W = CONHOH or COOH; R1 and R2 = H or an organic residue; R3 = organic group; Q = secondary or tertiary acyclic or cyclic amido group) and their pharmaceutically acceptable salts, solvates, and hydrates are disclosed as inhibitors of matrix metalloproteinases (MMPs), and of the release of tumor necrosis factor-alpha (TNF) from cells. The compds. are

&lt;12/04/2007&gt;

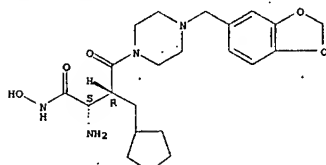
Erich Leese

therefore useful in the prevention, control and treatment of diseases in which MMPs or TNF are involved, especially tumoral and inflammatory diseases. Processes for their preparation, and pharmaceutical compns. containing them are also described. For instance, the intermediate 4(S)-(benzyloxycarbonyl)-1-(tert-butoxycarbonyl)-3(R)-isobutylsuccinidin-2-one (II; preparation given) was subjected to a sequence of ring opening/amidation with piperidine, followed by hydrogenolytic deprotection of the benzyl ester, amidation with PhCH2ONH2.HCl, another hydrogenolysis of the benzyl ether, and acidic deprotection of the BOC-amino group, to give title compound III. The latter compound showed superior aqueous solubility (> 9.5 mg/mL at 25°), and had  $\lambda_{\text{max}}$  values as follows: MMP-1 0.088, MMP-2 0.29, and MMP-3 2.5, all in  $\mu\text{M}$ .

IT 220046-45-7P  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)  
(target compound; preparation of succinyl piperidinamides, morpholinamides, and piperazinamides as matrix metalloproteinase inhibitors)

RN 220046-45-7 CAPLUS  
CN 1-Piperazinebutanamide,  $\alpha$ -amino-4-(1,3-benzodioxol-5-ylmethyl)- $\beta$ -(cyclopentylmethyl)-N-hydroxy- $\gamma$ -oxo-, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

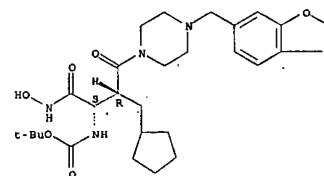
Absolute stereochemistry.



IT 220046-44-6P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(target compound; preparation of succinyl piperidinamides, morpholinamides, and piperazinamides as matrix metalloproteinase inhibitors)

RN 220046-44-6 CAPLUS  
CN Carbamic acid, [(1S,2R)-3-[(4-(1,3-benzodioxol-5-ylmethyl)-1-piperazinyl)-2-(cyclopentylmethyl)-1-[(hydroxyamino)carbonyl]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

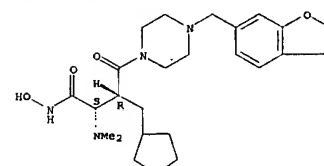
Absolute stereochemistry.



IT 220046-55-9P 220046-57-1P 220046-70-8P  
220046-82-2P 220046-88-8P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(target compound; preparation of succinyl piperidinamides, morpholinamides, and piperazinamides as matrix metalloproteinase inhibitors)

RN 220046-55-9 CAPLUS  
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)- $\beta$ -(cyclopentylmethyl)- $\alpha$ -(dimethylamino)-N-hydroxy- $\gamma$ -oxo-, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220046-57-1 CAPLUS  
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)- $\beta$ -(cyclopentylmethyl)-N-hydroxy- $\alpha$ -[[4-(methoxyphenyl)sulfonylamino]- $\gamma$ -oxo-, ( $\alpha$ S, $\beta$ R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

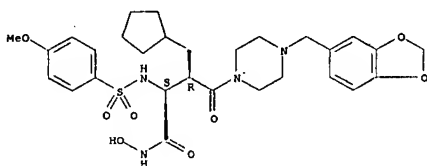
&lt;12/04/2007&gt;

Erich Leese

&lt;12/04/2007&gt;

Erich Leese

10/513699



RN 220046-70-8 CAPLUS

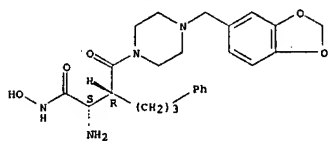
CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-N-hydroxy-γ-oxo-β-(3-phenylpropyl)-, (αS,βR)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220046-69-5

CMF C25 H32 N4 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 220046-82-2 CAPLUS

CN 1-Piperazinebutanamide, α-amino-4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, (αS,βR)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

&lt;12/04/2007&gt;

Erich Leese

10/513699

CM 2

CRN 76-05-1

CMF C2 H F3 O2



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD, ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER: 1979:604719 CAPLUS

DOCUMENT NUMBER: 91:204719

TITLE: Pharmaceutical compositions containing piperazinyl acylhydroxamic acid derivatives to treat inflammation or anaphylactic allergy conditions

Coutts, Ronald T.; Biggs, David F.; Wandelmaier, Frank W.; Semaka, Frank D.

Canadian Patents and Development Ltd., Can.

U.S., 5 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

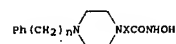
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4166116	A	19790828	US 1977-850825	19771111
CA 1095832	A1	19810217	CA 1978-315010	19781031
PRIORITY APPLN. INFO.:			US 1977-850825	A 19771111

OTHER SOURCE(S): MARPAT 91:204719

GI

QY  
I

AB Seven piperazinylacylhydroxamic acids I (X = straight or branched C1-3 alkylene, m = 0, 1, or 2, Y = a salt forming acid (when present)) derivs. were prepared by aminoesterification of the corresponding 1-monosubstituted piperazines and then converted to the HCl salts. The compds. showed antiinflammatory, antianaphylactic, and antidepressant activities. Thus, 2-methyl-3-[(1-(4-phenyl)piperazinyl)propionohydroxamic acid-HCl (71861-77-3)] inhibited carrageenan-induced edema volume by 23.5% 1 h after s.c. administration to rats, decreased egg albumin-induced anaphylaxis by 72% when given i.v. to rats (50 mg/kg), and protected 92% of reserpinized rats given 32 mg of the compound/kg. i.p.

IT 71861-78-4P 71861-81-9P

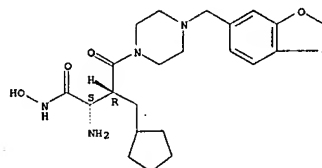
&lt;12/04/2007&gt;

Erich Leese

10/513699

CRN 220046-45-7  
CMF C22 H32 N4 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 220046-88-8 CAPLUS

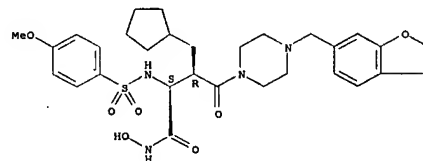
CN 1-Piperazinebutanamide, 4-(1,3-benzodioxol-5-ylmethyl)-β-(cyclopentylmethyl)-N-hydroxy-γ-oxo-, α-[(4-methoxyphenyl)sulfonyl]aminol-γ-oxo-, (αS,βR)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220046-57-1

CMF C29 H38 N4 O8 S

Absolute stereochemistry.



&lt;12/04/2007&gt;

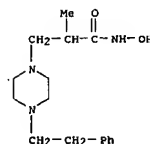
Erich Leese

10/513699

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and antiinflammatory and antianaphylactic activity of)

RN 71861-78-4 CAPLUS

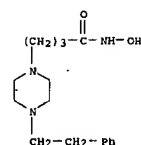
CN 1-Piperazinepropanamide, N-hydroxy-α-methyl-4-(2-phenylethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 71861-81-9 CAPLUS

CN 1-Piperazinebutanamide, N-hydroxy-4-(2-phenylethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

&lt;12/04/2007&gt;

Erich Leese